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November 27, 2002

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Commissioner for Patents
Washington, D.C. 20231

Art Unit: 1626

Re: U.S. Utility Patent Application
Appl. No. 09/814,123; Filed: March 22, 2001
For: **Aryl Substituted Pyrazoles, Triazoles and Tetrazoles, and the Use
Thereof**
Inventors: **HOGENKAMP *et al.***
Our Ref: **1861.1270001/JMC/THN**

Sir:

Transmitted herewith for appropriate action are the following documents:

1. Amendment and Reply Under 37 C.F.R. § 1.111; and
2. One (1) postcard.

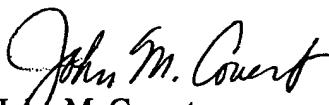
It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

Commissioner for Patents
November 27, 2002
Page 2

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.


John M. Covert
Attorney for Applicants
Registration No. 38,759

Enclosures

::ODMA\MHODMA\SKGF_DC1;79503;1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

HOGENKAMP et al.

Appl. No. 09/814,123

Filed: March 22, 2001

For: **Aryl Substituted Pyrazoles,
Triazoles and Tetrazoles, and the Use
Thereof**

Confirmation No. 2060

Art Unit: 1626

Examiner: Shameem, G.

Atty. Docket: 1861.1270001/JMC/THN

Amendment and Reply Under 37 C.F.R. §1.111

Commissioner for Patents
Washington, D.C. 20231

Sir:

In reply to the Office Action dated August 27, 2001 (PTO Prosecution File Wrapper Paper No. 11), Applicants submit the following Amendment and Remarks. This Amendment is provided in the following format:

- (A) A clean version of each replacement paragraph/section/claim along with clear instructions for entry;
- (B) Starting on a separate page, appropriate remarks and arguments. 37 C.F.R. § 1.111 and MPEP 714; and
- (C) Starting on a separate page, a marked-up version entitled: "Version with markings to show changes made."

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees

for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

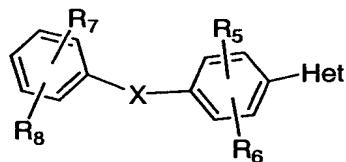
Amendment

In the Claims:

Please cancel claims 11-14, 18-21, 26 and 27 without prejudice or disclaimer.

Please substitute the following claim 1 for the pending claim 1:

1. (Twice amended) A compound having the Formula *I*:

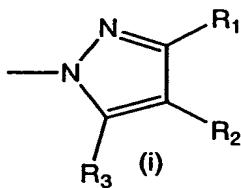


I

or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is one of O, S or CH₂;

Het is



R₁ is selected from the group consisting of hydrogen, optionally substituted alkyl, heteroaryl optionally substituted with one or more groups independently selected from the group consisting of halo, halo(C₁₋₆)alkyl, hydroxy(C₁₋₆)alkyl, aminō(C₁₋₆)alkyl, hydroxy, nitro, C₁₋₆ alkyl, C₁₋₆ alkoxy, aminocarbonyl, carbamoyloxy, C₁₋₆ alkylsulfonylamino, C₁₋₆ acyl and amino, C(O)R₁₀, CH₂C(O)R₁₀, S(O)R₁₀, and SO₂R₁₀;

R_2 and R_3 are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, cyano, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, carboxyalkyl, alkylamino, dialkylamino, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, aralkylaminocarbonyl, alkylcarbonylamino, arylcarbonylamino, aralkylcarbonylamino, alkylcarbonyl, aminosulfonyl, alkylaminosulfonyl, and alkylsulfonyl;

R_5 , R_6 , R_7 , and R_8 are independently selected from the group consisting of hydrogen, halo, haloalkyl, alkyl, alkenyl, alkynyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, alkoxyalkyl, nitro, amino, ureido, cyano, acylamino, amide, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, carbonylamido and alkylthiol;

R_{10} is selected from the group consisting of amino, alkyl, alkenyl, alkynyl, OR_{11} , alkylamino, dialkylamino, alkenylamino, dialkylaminoalkenyl, cycloalkyl, heterocycle, heteroaryl, aryl, aralkyl, arylalkenyl, arylalkynyl, and cycloalkylalkylamino, all of which are optionally substituted; and

R_{11} is selected from the group consisting of hydrogen, optionally substituted alkyl, and an alkali metal.

Please substitute the following claim 15 for the pending claim 15:

15. (Twice Amended) A compound of claim 1, wherein:

R_1 is $C(O)R_{10}$, $CH_2C(O)R_{10}$, or SO_2R_{10} ;

X is O or S;

R_{10} is amino, optionally substituted C_1 - C_6 alkyl, or a heterocycle selected from the group consisting of N-morpholinyl, N-pyrrolidinyl and N-piperazinyl;

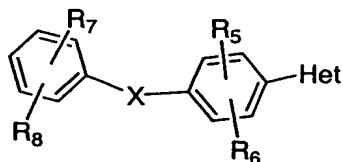
R_2 , and R_3 are independently hydrogen, C_1 - C_6 alkyl, C_1 - C_6 alkylthio or C_1 - C_6 alkylsulfinyl,

R_5 and R_6 are as defined in claim 1, and

R_7 and R_8 are independently selected from the group consisting of hydrogen, halo, halo(C_1 - C_6)alkyl, C_1 - C_6 alkyl, hydroxy(C_1 - C_6)alkyl, amino(C_1 - C_6)alkyl, carboxy(C_1 - C_6)alkyl, alkoxy(C_1 - C_6)alkyl, nitro, amino, C_1 - C_6 acylamino, amide, hydroxy, thiol, C_1 - C_6 acyloxy, C_1 - C_6 alkoxy, carboxy, carbonylamido and C_1 - C_6 alkylthiol.

Please substitute the following claim 16 for the pending claim 16:

16. (Twice Amended) A compound of Formula *I*:

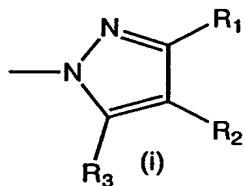


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or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is O or S;

Het is



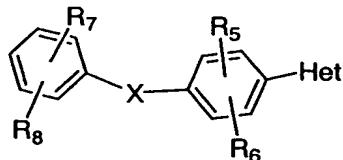
R₁ is C(O)R₁₀, CH₂C(O)R₁₀, or SO₂R₁₀ wherein R₁₀ is amino, alkyl, N-morpholinyl, N-pyrrolidinyl or N-piperazinyl, all of which are optionally substituted;

R₂ and R₃ are independently hydrogen, C₁-C₆ alkyl, C₁-C₆ alkylthio or C₁-C₆ alkylsulfinyl; and

R₅, R₆, R₇ and R₈ are independently selected from the group consisting of hydrogen, halo, halo(C₁-C₆)alkyl, C₁-C₆ alkyl, hydroxy(C₁-C₆)alkyl, amino(C₁-C₆)alkyl, carboxy(C₁-C₆)alkyl, alkoxy(C₁-C₆)alkyl, nitro, amino, C₁-C₆ acylamino, amide, hydroxy, thiol, C₁-C₆ acyloxy, C₁-C₆ alkoxy, carboxy, carbonylamido and C₁-C₆ alkylthiol.

Please substitute the following claim 22 for the pending claim 22:

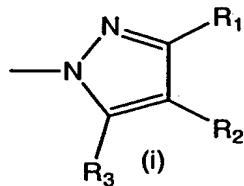
22. (Twice Amended) A compound of Formula *I*:



or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is O or S;

Het is



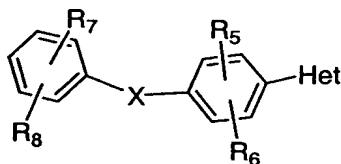
R₁ is C(O)R₁₀, wherein R₁₀ is amino, N-morpholinyl, N-pyrrolidinyl or N-piperazinyl, all of which are optionally substituted;

R₂ and R₃ are independently hydrogen, C₁-C₆ alkyl, C₁-C₆ alkylthio or C₁-C₆ alkylsulfinyl; and

R₅, R₆, R₇ and R₈ are independently selected from the group consisting of hydrogen, halo, halo(C₁-C₆)alkyl, C₁-C₆ alkyl, hydroxy(C₁-C₆)alkyl, amino(C₁-C₆)alkyl, carboxy(C₁-C₆)alkyl, alkoxy(C₁-C₆)alkyl, nitro, amino, C₁-C₆ acylamino, amide, hydroxy, thiol, C₁-C₆ acyloxy, C₁-C₆ alkoxy, carboxy, carbonylamido and C₁-C₆ alkylthiol.

Please substitute the following claim 25 for the pending claim 25:

25. (Once amended) A compound having the Formula I:

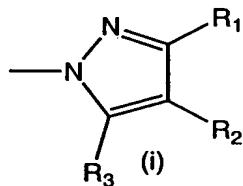


I

or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is NR₉C(O) or C(O)NR₉, where R₉ is hydrogen or C₁-C₁₀ alkyl;

Het is



R₁ is SO₂R₁₀;

R₂ and R₃ are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, cyano, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, carboxyalkyl, alkylamino, dialkylamino, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, aralkylaminocarbonyl, alkylcarbonylamino, arylcarbonylamino, aralkylcarbonylamino, alkylcarbonyl, aminosulfonyl, alkylaminosulfonyl, and alkylsulfonyl;

R₅, R₆, R₇, and R₈ are independently selected from the group consisting of hydrogen, halo, haloalkyl, alkyl, alkenyl, alkynyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, alkoxyalkyl, nitro, amino, ureido, cyano, acylamino, amide, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, carbonylamido and alkylthiol;

R₁₀ is selected from the group consisting of amino, alkyl, alkenyl, alkynyl, OR₁₁, alkylamino, dialkylamino, alkenylamino, dialkylaminoalkenyl, cycloalkyl, heterocycle, heteroaryl, aryl, aralkyl, arylalkenyl, arylalkynyl, and cycloalkylalkylamino, all of which are optionally substituted; and

R₁₁ is selected from the group consisting of hydrogen, optionally substituted alkyl, and an alkali metal.

Remarks

Reconsideration of this Application is respectfully requested.

Applicants respectfully point out that the forms PTO-1449 accompanying Applicants' Information Disclosure Statement and First Supplemental Information Disclosure Statement, filed December 13, 2001 and December 19, 2001, respectively, have not been initialed and signed to indicate that the Examiner has considered the cited art and made said consideration of record. Applicants respectfully request the Examiner to provide copies of the initialed and signed forms.

Upon entry of the foregoing amendment, claims 1-10, 15-17 and 22-25 are pending in the application, with claims 1, 16, 22 and 25 being the independent claims. Claims 11-14, 18-21, 26 and 27 have been canceled without prejudice or disclaimer. Canceled claim 11 and amended claim 1 are coequal. Applicants reserve the right to file one or more continuing applications directed to the subject matter of canceled claims 12-14, 18-21, 26 and 27 and to the subject matter removed from pending claims 1-10, 15-17 and 22-25 by the above amendment.

Claims 1, 15, 16, 22 and 25 are sought to be amended. Support for the amendments can be found in the original specification and claims as filed. These changes are believed to introduce no new matter, and their entry is respectfully requested. Specifically, each of the indicated claims has been amended such that Het in Formula I is a pyrazolyl group. Applicants submit that no new matter has been introduced by this amendment since deletion of individual members of a Markush expression does not constitute new matter. *See In re Johnson and Farnham*, 558 F.2d 1008, 1019, 194 U.S.P.Q. 187, 196 (CCPA 1977). Additionally, claims 1 and 25 have been amended to clarify that the members of the Markush group that constitute R₁₀

are optionally substituted. Preferred values of R_{10} are found in the specification, at page 7, paragraph [0033], and are described as optionally substituted. It follows logically that if one value of R_{10} is, e.g., amino, and a preferred value of R_{10} is optionally substituted amino, then the broader, not necessarily preferred definition of R_{10} must include optionally substituted amino. Thus, no new matter has been introduced by this amendment.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Restriction/Election

Claims 1-27 are subject to a restriction requirement as described in the Office Action mailed July 1, 2002 (Paper No. 9). Applicants filed a reply on July 31, 2002 (Paper No. 10) traversing the restriction and making a provisional election. However, solely to expedite prosecution, Applicants have herein amended the claims to limit "Het" in **Formula I** to a pyrazolyl moiety. The claims as currently amended read on compounds sharing a structural core and sharing utility, namely, they are sodium channel blockers.

The Examiner asserts that Applicants' arguments traversing the restriction were based on MPEP §§ 803 and 803.2, but that 35 U.S.C. § 121 is the singular basis for the restriction. The Examiner further asserts that 35 U.S.C. § 121 makes clear that restriction may be required in certain applications and that the Director has the right to make such a determination.

While it is not disputed that 35 U.S.C. § 121 is the statutory basis for restriction, Applicants traverse the Examiner's requirement of restriction in this case.

In their July 31 remarks, Applicants cited *In re Weber*, 580 F.2d 455 (CCPA 1978) for the holding that restriction practice is not applicable to a single claim. "As a general proposition, an applicant has a right to have *each* claim examined on the merits. . . . If, however, a single claim is required to be divided up and presented in several applications, that claim would never be considered on its merits." *Weber*, 580 F.2d at 458 (emphasis in original). "Ever since [1870], at least, the expression used in § 121, 'two or more . . . inventions are claimed,' has connoted separate claims to separate inventions. It has no reference to generic or broad claims which 'embrace' . . . or 'cover' . . . two or more inventions. . . . [Section 121] says 'claimed,' and that I take to mean what it has always referred to in the terminology of the patent law, a 'claim'. . . ." *Id.* at 459-60 (Rich, J., concurring).

In contravention of this pronouncement by the author of the 1952 Patent Act, the Examiner has defined six inventions in the captioned application, which definitions require dividing individual claims into separate applications. Specifically, both claims 1 and 17 have been divided between Groups I and II. Inasmuch as the restriction requires division of individual claims into separate applications, Applicants respectfully submit that the restriction is improper.

In requiring restriction, the Examiner stated that "the products of groups I to VI differ materially in structure and in element from each other and are capable of supporting their own patents." He additionally asserted that "to not restrict would impose a burden in the examination of this application." The Examiner placed claims 1-14 and 17 in Group I, and claim 25 in Group V. However, the genus of claim 25 shares with claim 1 not only a structural core but definitions of substituents R₂-R₃, R₅-R₈ and R₁₀-R₁₁, and R₁ in claim 25 is a subset of R₁ in claim 1. The only difference between the two genera (other than the narrower scope of R₁ in claim 25) is

that X in claim 1 is O, S or CH₂, while X in claim 25 is NR₉C(O) or C(O)NR₉, wherein R₉ is hydrogen or C₁₋₁₀ alkyl. Applicants respectfully disagree that this difference constitutes such a material difference in structure and in element that extending the search to include the two additional definitions of X would impose a burden on the Examiner.

Further, the Examiner placed claims 1-14 and 17 in Group I, claims 1, 15-17 and 24 in Group II, and claims 22-23 in Group IV. Applicants respectfully point out that claim 15 depends from claim 1, and that claim 16, while independent, could be rewritten as depending from claim 1 without altering its scope. Claim 24 depends from claim 15. Similar remarks apply to Group IV: claim 22 could be rewritten to depend from claim 1 without altering its scope, and claim 23 depends from claim 22. The Examiner has made no statement, save the conclusory remark quoted above, explaining how claims that all either depend from or could depend from a single claim can be said to differ materially in structure and in element. Similarly, the Examiner has made no statement explaining how searching Groups II and IV would present any additional burden over searching Group I. Indeed, because the claims of Groups I, II and IV are entirely within the scope of claim 1, it is not clear how the Examiner could examine Group I without necessarily—if inadvertently—examining Groups II and IV as well.

The requirement of restriction under these circumstances is tantamount to a rejection for improper Markush grouping. As discussed above, the subject matter of the claims of Groups I, II and IV falls within the scope of claim 1. Thus, the Examiner is effectively dividing the Markush group of claim 1 into three different groups of subject matter asserted to be patentably distinct. Applicants respectfully traverse this *de facto* rejection.

It is improper to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. MPEP § 803.02. The test for proper joinder of invention within a claim is whether unity of invention exists. Unity of invention exists for compounds when the compounds share a structural core and share a community of properties, such that the grouping of such compounds together is not repugnant to the principles of scientific classification. *See In re Harnisch*, 631 F.2d 716, 722, 206 U.S.P.Q. 300, 305 (CCPA 1980). Different classification is not a sufficient condition to require restriction.

The claims, as currently amended solely to expedite the prosecution of the captioned application, are directed to compounds that share the structural core represented by Formula I, above (and at specification, p. 5, paragraph [0021]), where Het is a pyrazolyl moiety. The compounds also share utility, namely, they are sodium channel blockers. *See* specification, at p. 3, paragraph [0010]. Thus, the claims of Groups I, II and IV are directed to subject matter for which unity of invention exists. Therefore, compounds of claim 1—and by extension, claims 15, 16 and 24, and claims 22 and 23—are defined by a proper Markush group. *See* MPEP § 803.02.

In light of the foregoing remarks, reconsideration and withdrawal of the restriction are respectfully requested. Additionally, consideration of withdrawn claims 15, 16 and 22-25, as amended, and of the subject matter withdrawn from claims 1-10 and 17, is respectfully requested.

In the July 1 Office Action, the Examiner required, in addition to restriction of the invention to one of six groups, an election of species. The Examiner stated that upon such election, "a generic concept inclusive of the elected species [would] be identified by the Examiner for examination along with the elected species." In Applicants' July 31 Remarks, the species 1-(4-phenoxyphenyl)-

1*H*-pyrazole-3-carboxamide was provisionally elected with traverse. The Examiner asserts that the July 1 Office Action stated the generic concept as being a compound of Formula *I* wherein X is O or S, Het is heteroaryl selected from the group consisting of pyrazoles (i), R₁ is selected from the group consisting of hydrogen and optionally-substituted alkyl, R₂ and R₃ are as claimed, and R₅, R₆, R₇ and R₈ are as defined. Applicants respectfully point out that no such definition of the generic concept was proffered by the Examiner in the referenced Office Action. Moreover, the generic concept identified by the Examiner does not include the elected species. Specifically, the Examiner's definition of R₁ (which corresponds to the 3-position of 1*H*-pyrazole) as hydrogen or optionally-substituted alkyl does not encompass the carboxamide group of the elected species. Finally, it is for the Applicant, not the Examiner, to define that which Applicant claims as his invention.

Solely to expedite prosecution, Applicants have voluntarily amended the pending claims such that Het is (i), a pyrazolyl, and those claims in which Het is other than a pyrazolyl have been canceled. Additionally, the claims directed to methods and to radiolabeled compounds, even those in which Het is a pyrazolyl moiety, have been canceled. Applicants respectfully submit that the generic concept is defined by the Formula *I* wherein Het is (i), i.e., a pyrazolyl; X is O, S, CH₂, NR₉C(O) or C(O)NR₉, wherein R₉ is defined as in claim 25; and R₁-R₃, R₅-R₈ and R₁₀-R₁₁ are as defined in claim 1.

Additionally, Applicants respectfully submit that the Examiner has not conducted examination pursuant to the guidelines set forth in the MPEP. MPEP § 803.02 requires that if examination of a Markush claim can be made without *serious burden*, the examiner must examine all the members of the Markush group even if the examiner believes they are directed to independent and distinct inventions. Moreover,

after an election of species, the examiner must fully examine the Markush group with respect to the elected species and further to determine patentability.

The Office Action Summary indicates that claims 1-14 and 17 are rejected, while the Detailed Action only objects to claims 1-14 and 17 as containing non-elected subject matter and states that claims drawn to the elected invention—as identified by the Examiner—"would appear allowable." However, the Examiner has not cited any art to justify not extending the examination beyond the Markush group with respect to the elected species. Applicants respectfully request that the Examiner clarify whether the claims are objected to, or rejected. Further, Applicants respectfully request that the Examiner conduct examination of the entire Markush group according to MPEP § 803.02 unless and until art is cited in support of limiting the examination.

Nor, as discussed above, has the Examiner explained how searching claims 15, 16 and 22-25 imposes a *serious burden* beyond examining claim 1. Applicants respectfully request examination of all pending claims.

Objection

Claims 1-14 and 17 are objected to as allegedly containing non-elected subject matter. Applicants respectfully submit that withdrawal from consideration of subject matter from these claims was improper for the reasons already stated. Claims 11-14 are canceled as discussed above. Consideration of all of the subject matter of claims 1-10 and 17 is respectfully requested.

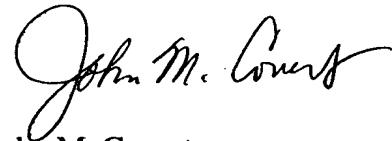
Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



John M. Covert
Attorney for Applicants
Registration No. 38,759

Date: Nov. 27, 2002

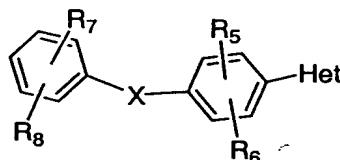
1100 New York Avenue, N.W.
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(202) 371-2600

Version with markings to show changes made

Claims 11-14, 18-21, 26 and 27 have been canceled.

Claims 1, 15, 16, 22 and 25 have been amended as follows:

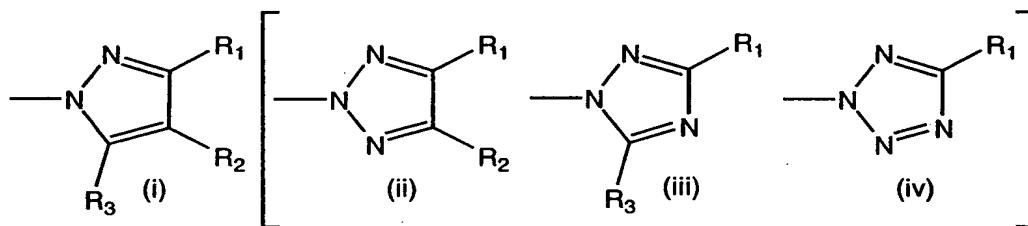
1. (Twice amended) A compound having the Formula I:



I

or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is one of O, S[₁₋₃], NR₉,] or CH₂[₁₋₃, where R₉ is hydrogen or C₁-C₁₀ alkyl];
Het is[a heteroaryl selected from the group consisting of]



R₁ is selected from the group consisting of hydrogen, optionally substituted alkyl, heteroaryl optionally substituted with one or more groups independently selected from the group consisting of halo, halo(C₁₋₆)alkyl, hydroxy(C₁₋₆)alkyl, amino(C₁₋₆)alkyl, hydroxy, nitro, C₁₋₆ alkyl, C₁₋₆ alkoxy, aminocarbonyl, carbamoyloxy, C₁₋₆ alkylsulfonylamino, C₁₋₆ acyl and amino, C(O)R₁₀, CH₂C(O)R₁₀, S(O)R₁₀, and SO₂R₁₀;

R₂ and R₃ are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, cyano, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, carboxyalkyl, alkylamino, dialkylamino, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, aralkylaminocarbonyl, alkylcarbonylamino, arylcarbonylamino, aralkylcarbonylamino, alkylcarbonyl, aminosulfonyl, alkylaminosulfonyl, and alkylsulfonyl;

R₅, R₆, R₇, and R₈ are independently selected from the group consisting of hydrogen, halo, haloalkyl, alkyl, alkenyl, alkynyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, alkoxyalkyl, nitro, amino, ureido, cyano, acylamino, amide, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, carbonylamido and alkylthiol;

R₁₀ is selected from the group consisting of amino, alkyl, alkenyl, alkynyl, OR₁₁, alkylamino, dialkylamino, alkenylamino, dialkylaminoalkenyl, cycloalkyl, heterocycle, heteroaryl, aryl, aralkyl, arylalkenyl, arylalkynyl, and cycloalkylalkylamino, all of which are optionally substituted; and

R₁₁ is selected from the group consisting of hydrogen, optionally substituted alkyl, and an alkali metal; and

provided that:

- 1) when Het is (ii), and X is O, then R₁₀ is not alkyl, aralkyl, aryl or OR₁₁;
- 2) when Het is (i) or (ii), then X is not NR₉;
- 3) when Het is (iii), then X is not CH₂; and
- 4) when Het is (iii), and X is O, then R₁₀ is not OR₁₁].

15. (Twice Amended) A compound of claim 1, wherein:

[Het is (i), (ii), (iii) or (iv);]

R₁ is C(O)R₁₀, CH₂C(O)R₁₀, or SO₂R₁₀;

X is O or S;

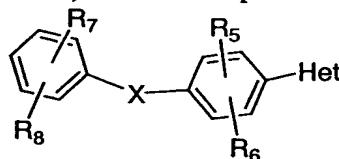
R₁₀ is amino, optionally substituted C₁-C₆ alkyl, or a heterocycle selected from the group consisting of N-morpholinyl, N-pyrrolidinyl and N-piperazinyl;

R₂, and R₃ are independently hydrogen, C₁-C₆ alkyl, C₁-C₆ alkylthio or C₁-C₆ alkylsulfinyl,

R₅ and R₆ are as defined in claim 1, and

R₇ and R₈ are independently selected from the group consisting of hydrogen, halo, halo(C₁-C₆)alkyl, C₁-C₆ alkyl, hydroxy(C₁-C₆)alkyl, amino(C₁-C₆)alkyl, carboxy(C₁-C₆)alkyl, alkoxy(C₁-C₆)alkyl, nitro, amino, C₁-C₆ acylamino, amide, hydroxy, thiol, C₁-C₆ acyloxy, C₁-C₆ alkoxy, carboxy, carbonylamido and C₁-C₆ alkylthiol.

16. (Once Amended) A compound of Formula I:

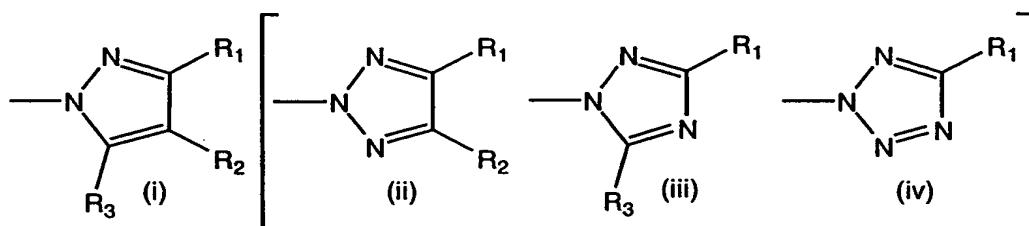


I

or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is O or S;

Het is [a heteroaryl selected from the group consisting of]



R₁ is C(O)R₁₀, CH₂C(O)R₁₀, or SO₂R₁₀ wherein R₁₀ is amino, alkyl, N-morpholinyl, N-pyrrolidinyl or N-piperazinyl, all of which are optionally substituted;

R₂ and R₃ are independently hydrogen, C₁-C₆ alkyl, C₁-C₆ alkylthio or C₁-C₆ alkylsulfinyl; and

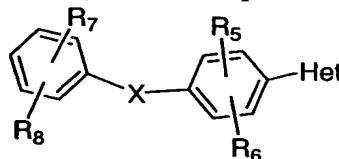
R₅, R₆, R₇ and R₈ are independently selected from the group consisting of hydrogen, halo, halo(C₁-C₆)alkyl, C₁-C₆ alkyl, hydroxy(C₁-C₆)alkyl, amino(C₁-C₆)alkyl, carboxy(C₁-C₆)alkyl, alkoxy(C₁-C₆)alkyl, nitro, amino, C₁-C₆

acylamino, amide, hydroxy, thiol, C₁-C₆ acyloxy, C₁-C₆ alkoxy, carboxy, carbonylamido and C₁-C₆ alkylthiol[;

provided that:

- 1) when Het is (ii), and X is O, then R₁₀ is not alkyl, aralkyl, aryl or OR₁₁; and
- 2) when Het is (iii), and X is O, then R₁₀ is not OR₁₁].

22. (Twice Amended) A compound of Formula I:

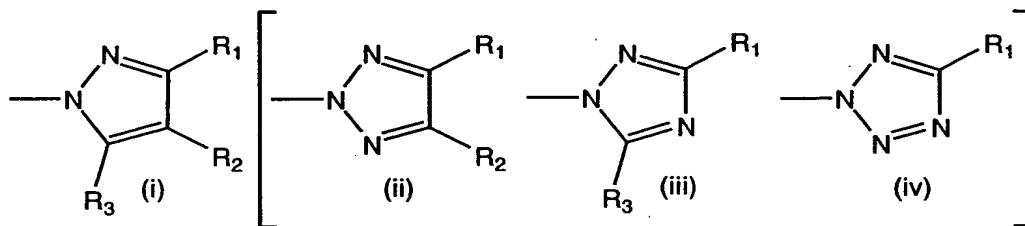


I

or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is O or S;

Het is[a heteroaryl selected from the group consisting of]



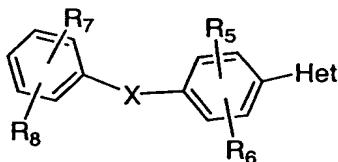
R₁ is C(O)R₁₀, wherein R₁₀ is amino, N-morpholinyl, N-pyrrolidinyl or N-piperazinyl, all of which are optionally substituted;

R₂ and R₃ are independently hydrogen, C₁-C₆ alkyl, C₁-C₆ alkylthio or C₁-C₆ alkylsulfinyl; and

R₅, R₆, R₇ and R₈ are independently selected from the group consisting of hydrogen, halo, halo(C₁-C₆)alkyl, C₁-C₆ alkyl, hydroxy(C₁-C₆)alkyl, amino(C₁-C₆)alkyl, carboxy(C₁-C₆)alkyl, alkoxy(C₁-C₆)alkyl, nitro, amino, C₁-C₆ acylamino, amide, hydroxy, thiol, C₁-C₆ acyloxy, C₁-C₆ alkoxy, carboxy, carbonylamido and C₁-C₆ alkylthiol.

25. (Once amended)

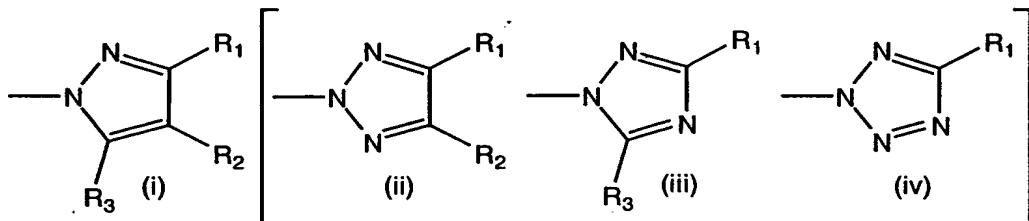
A compound having the Formula I:



I

or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is $\text{NR}_9\text{C}(\text{O})$ or $\text{C}(\text{O})\text{NR}_9$, where R_9 is hydrogen or $\text{C}_1\text{-C}_{10}$ alkyl;
Het is [a heteroaryl [selected from the group consisting of]



R_1 is SO_2R_{10} ;

R_2 and R_3 are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, cyano, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, carboxyalkyl, alkylamino, dialkylamino, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, aralkylaminocarbonyl, alkylcarbonylamino, arylcarbonylamino, aralkylcarbonylamino, alkylcarbonyl, aminosulfonyl, alkylaminosulfonyl, and alkylsulfonyl;

R_5 , R_6 , R_7 , and R_8 are independently selected from the group consisting of hydrogen, halo, haloalkyl, alkyl, alkenyl, alkynyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, alkoxyalkyl, nitro, amino, ureido, cyano, acylamino, amide, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, carbonylamido and alkylthiol;

R_{10} is selected from the group consisting of amino, alkyl, alkenyl, alkynyl, OR_{11} , alkylamino, dialkylamino, alkenylamino, dialkylaminoalkenyl, cycloalkyl, heterocycle, heteroaryl, aryl, aralkyl, arylalkenyl, arylalkynyl, and cycloalkylalkylamino, all of which are optionally substituted; and

R_{11} is selected from the group consisting of hydrogen, optionally substituted alkyl, and an alkali metal.

Applicants: HOGENKAMP *et al.*

Application No.: 09/814,123

Filed: March 22, 2001

For: Aryl Substituted Pyrazoles, Triazoles and Tetrazoles, and the Use Thereof

Due Date: November 27, 2002

Art Unit: 1626

Examiner: Shameem, G.

Docket: 1861.1270001

Atty: JMC/THN

When receipt stamp is placed hereon, the USPTO acknowledges receipt of the following documents:

1. SKGF Cover Letter;
2. Amendment and Reply Under 37 C.F.R. § 1.111; and
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